What Are You Going to Conquer with the Spear?

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Almost everyone in China knows this story, even elementary school pupils: Once upon a time, there was a weapon salesman claiming with confidence to one crowd that all his spears were capable of piercing every shield that existed in the world, then he turned around and told the other crowd mysteriously that all his shields were not penetrable. A bystander who heard both claims asked him, "How about stabbing your shields with your spears?" It was indeed an unexpected question that made the eloquent salesman mute right on the spot. Since then, the Chinese people have called contradiction as "mao-dun", which literally means "the spear (pronounced as "mao") and shield (pronounced as "dun")".

A lot of people in China, including researchers in the field of life sciences, scientific policy-makers, governmental funding agencies, and even the general public, have been made to believe that "functional genomics" is the way to go for genomic research and it provides the single most powerful tool set for future life sciences. It is neither genomics nor genome biology, and certainly not the most expensive tool of genomics, called DNA sequencing. Modern "weapon salesmen" are much smarter now than their ancient counterparts, having learnt the hard lesson—never contradict your own sales advertisement. Just to be safe, they now only sell "spears" or "shields", not both at the same time. "Functional genomics" has been one of such powerful weapons on sale. Regardless the social purpose of this somewhat vicious amputation of an emerging modern scientific discipline, the sale has been very successful by any modern measurement, overriding genomics, and becoming an invincible "spear" to draw full attention from many crowds. The essence of a sweeping win over other versions of genomics and its tools is to dissever the "soul" or "spirit" (function) from its "body" (gene). Isn't it a familiar trick that we have seen all the time and in most of the places?

Is "functional genomics" what genomics are all about? The answer is certainly not, especially when one takes a deep breath and thinks in a logical way. First, there is no such a thing called "non-functional genomics", or even "structural genomics"; it is therefore pointless to create a particular phrase, called "functional genomics", to distinguish the non-existent, unless someone really has an axe to grind. It might be useful in reality for some commercial entities to attract their investors' and shareholders' attention with ever-fancier technological terms but it is definitely not logical for academic researchers. Genes are functional units of genomes; gene products may possess certain definable fucntions but never all of them. Genomics provides concepts and tools to study genes, including their functions, not just sequences of genes as deliberately painted by advocators of functional genomics. Second, functional genomics seems emphasizing only the tools for studying gene functions, providing an *ex parte* view on genomic conception and technology. Expressed sequence tags (ESTs) were once claimed as "functional parts of genes". Gene expression profiling is certainly not a type of functional studies by such a definition; it merely acquires patterns of gene expression in a functional unit of life forms—the cell. Proteomic tools, such as mass spectrometry and x-ray crystallography, are also exclusive; they provide similar patterns of protein expression and structural details of a gene's proteinaceous product. The same can be said about microarray-based tools. None of the above mentioned techniques addresses the function of genes. What are the functional genomics tools? The answers seem to taper only classical techniques of biochemistry and molecular biology as well as transgenics, the yeast two-hybrid systems, and perhaps, a recent hope, the RNAi approach. These are all capable of appraising functions of gene products but in rather a limited scope and scale, and their rate of success in explaining gene functions is so far proven low (generously speaking less than 10%). Functional genomics thus removes the two basic characteristics from genomics—as a collection of large-scale technologies and a discovery-driven research discipline.

The incurable consequences in ignoring other important, yet "non-functional genomic" techniques, such as genome (DNA) sequencing, microarray, and genotyping, are at least three folds. First, genomicists in China, without expected funding, have been left alone to draw on other people's data for their

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own research field. A "data beggar" seemed not as so disgraceful as a food beggar. It reminds us the attitude of a dispirited legendary figure, Kong Yi-Ji, described by Chinese litterateur Lu Xun in his famous novel, who believed scholars should not feel dishonored when stealing books. Nevertheless, when basic genomic information and the tools to acquire it are all in other people's hands, any original innovation is deemed rare. Second, genomic technologists in China have been discouraged to work on the most profitable regime of equipment and reagent development, even when DNA sequencers and relevant reagents are about to enter clinical diagnostic markets within this coming decade. What is more disastrous is the fact that DNA sequencing and related technology has turned out to be an essential laboratory technique in generating basic molecular biology information. Not a single molecular biology laboratory claims not to sequence DNA, not even the "functional genomics" advocators' laboratories. Why do they not even try to pretend? Finally, many Chinese biologists working in diverged fields of biological research have been wondering silently if their favorite genomes ever have any chance to be sequenced. Perhaps, some of them have tried to send in grant applications to do so and the answer from any responsible party must have been disappointing so far. Unless a bold measure could be made to borrow a large sum of money in tens of million yuan (a few million USD), it has not been solicitated by any governmental funding agencies that genome sequencing projects are choices of genomic or even biological reserch fundings. It was whispered that the money for silkworm and rice (*indica*) genomes sequenced in China was loaned. However, it has been widely believed that the funding was from the same "pot" for functional genomics study in China in tens of millions. One should really be wondering "what have you been stabbing with your spears—the functional genomics spear—if you are not studying (if sequencing is too primitive an operation) genomes?" If you are not sequencing a genome, where do you obtain the basic genomic information for biological studies? How do you compete with others who have sequence information already in hands? Claiming "First in China"?

What has been gratifying is that a series of publications on the silkworm and rice (both *indica* and*japonica*) genome projects, as well as on a chicken polymorphism project, have come into sight recently and the efforts have been led by Chinese scientists. It is an announcement that offers hope for future genome projects proposed in China. Together with the new funding cycle of scientific research, "the Eleventh Five-Year Plan", we hope that the "all-conquering spear"—genomic technology will contribute more to the scientific advancement in China. What are you going to conquer with your spears in the future if you regret a miscalculation? We encourage open discussions on what are the next few organisms to be sequenced by Chinese scientists. Could we organize a concerted effort and come up with a list of such organisms for the future? Candidate genomes for yet larger scale sequencing are certainly not in short of supply, which should include those of major crops, domestic animals, invading species, and numerous species that are vital for energy-generation and environmental conservations. It is of importance to have a common understanding about genome biology and genomic technology as well as a concrete plan to move genome biology to every field of biology.

Appendix—Recent Prominent Genomic Publications Contributed by Chinese Scientists
(including major joint efforts and for metazoan genomes only)

Project	Publication
Human Genome	1. The International Human Genome Sequencing Consortium. 2001. Initial sequencing and analysis of the human genome. *Nature* 409: 860-921.
	2. The International Human Genome Sequencing Consortium. 2004. Finishing the euchromatic sequence of the human genome. *Nature* 431: 931-945.
Rice Genome	1. Yu, J., *et al.* 2002. A draft sequence of the rice genome (*Oryza sativa* L. ssp. *indica*). *Science* 296: 79-92.
	2. Zhao, Q., *et al.* 2002. A fine physical map of the rice chromosome 4. *Genome Res.* 12: 817-823.
	3. Feng, Q., *et al.* 2002. Sequence and analysis of rice chromosome 4. *Nature* 420: 316-320.
	4. Yu, J., *et al.* 2005. The genomes of *Oryza sativa*: a history of duplications. *PLoS Biol.* 3: e38.
Silkworm Genome	Xia, Q., *et al.* 2004. A draft sequence for the genome of the domesticated silkworm (*Bombyx mori*). *Science* 306: 1937-1940.
Chicken Genome	1. Hillier, L.W, *et al.* 2004. Sequence and comparative analysis of the chicken genome provide unique perspectives on vertebrate evolution. *Nature* 432: 695-716.
	2. Wong, G.K., *et al.* 2004. A genetic variation map for chicken with 2.8 million single-nucleotide polymorphisms. *Nature* 432: 717-722.